UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,011	08/07/2001	John R. DePhillipo	E0543-00011	1968

8933 7590 10/31/2006

DUANE MORRIS, LLP
IP DEPARTMENT
30 SOUTH 17TH STREET
PHILADELPHIA, PA 19103-4196

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	09/924,011	DEPHILLIPO ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-17,20-27,30-32,63 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-17, 20-27, 30-32 and 63-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 4/11/05 has been acknowledged.

Claims 1, 14-17,20-27, 30-33 and 63-64 are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Earlier, the applicant elected combination of two disorder-associated polymorphism (DAP) is gene encoding Vitamin D receptor and Interleukin-6, wherein the Vitamin D receptor DAP comprises occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor, wherein the Interleukin-6 DAP comprises occurrence of a cytosine residue at position -1 74 of the interleukin 6 gene promoter.

Claim 64 is objected to because the subject matter of instant claims is drawn to non-elected inventions(s).

Claim Rejections - 35 USC § 112

Claims 1, 4-17, 20-27, 30-32 and 63-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the office action mailed on 6/17/05.

Response to arguments

The applicant argument regarding written description issue on pages 7-9 of response filed on 12/22/05 has been fully considered. The applicant argues that the specification teaches that the relevant polymorphism(s) are those that are known to be associated with a disorder in one of the specified genes. The applicant argues that the precise identity of the polymorphism and the disorder associated with it are immaterial and it is the fact that the association between the polymorphism and the disorder exists that is material to the claimed method. The applicant furhter argues that it is well within the level of skill of an ordinary worker in this field to perform a search of all polymorphisms that are associated with any particular gene and to identify those which have been associated with a disease or other pathological condition. The applicant argues that the office has mischaracterizing the Applicants' invention as merely a collection of specific polymorphisms that can be correlated with bone density of a patient, instead, the Applicants have invented a generic method of assessing occurrence of a certain type of polymorphisms that can be used to assess bone density conditions. The applicant argues that the characteristics of all of the polymorphisms in that class are i) that they occur in one of the genes recited in claim 1; and ii) that they have a known association with a disorder of any type. The applicant argues that a skilled artisan understands that this class of polymorphisms (like the class of "nails") includes both polymorphisms that are currently known and others for which the association between the polymorphism and a disorder will become known later (just as particular alloys, shapes, and colors of "nails" can be developed beyond the types already known). The applicant argues that the concentration on the nucleotide sequences of polymorphisms other than those listed in claim 1, is believed to be misplaced because the Applicants are not claiming the sequences themselves. The applicant argues that those sequences are simply information that is available in the art to skilled artisans, and the specification need not provide information that is available in the art to skilled artisans.

However, applicant's arguments are found not persuasive. The scope of invention as claim is not limited to Vit.D receptor and IL-6 but encompasses any two

known disorders-associated polymorphisms including [emphasis added] Vit.D receptor and IL-6 (see claim 64). Therefore the scope of invention as claimed encompasses DAPs other than Vit.D receptor and IL-6. Since the scope of invention as claimed is not limited to "two known disorders-associated polymorphisms selected from a group consisting of Vit.D receptor and IL-6", but reads upon any set of DAPs other than Vit.D receptor and IL-6. Furthermore the applicants argument that instant claims are not drawn to nucleic acid sequences has been found not persuasive because to practice the invention as claimed one skill in the art need the possession of oligonucleotides sequences for a particular DAP (see claim 14 and dependent claims). Therefore considering the applicant's disclosure it is unclear that applicants were in the possession of all nucleotides sequences required for the identification of DAPs under high stringency conditions.

In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. conserve motifs or domains). The specification fails to disclose representative number of species by structure and function encompassed by genus as claimed. Furthermore the genus as claimed encompasses structurally and functionally distinct members, which does not represent a common structure like "nail". Claiming all divergent species that achieve a result as contemplated by the application without defining the representative number of species by structure and function is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. "The written description requirement has several policy objectives. The essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re Barker, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977). Another objective is to put the public in possession of what the applicant claims as the invention. See Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998)." To satisfy

the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. *Possession may be shown by an actual reduction to practice, showing that the invention as claimed is "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention* (see January 5, 2001 Fed.Reg., Vo.66, No. 4, pp. 1099-11).

Since the specification fails to disclose nucleotides required to practice the instant invention, defined by structure and function, it is not possible to envision the claimed composition. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). In the instant case the DAP genes as claimed has been defined only by a statement of function that broadly encompasses "known disorder-associted polymorphism", which conveyed no distinguishing information about the identity of the DAP gene sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because scope of DAPs encompasses structurally and functionally unrelated genes.

Claims 1, 14-17, 20-27, 30-32 and 63-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the same reasons of record as set forth in the office action mailed on 6/17/05.

Response to arguments

The applicant arguments regarding enablement issue on pages 9-12 of response filed on 12/22/05 has been fully considered. The applicant argues that claims do not

recite a method of diagnosing existence of bone density condition, but rather a way of assessing relative susceptibility to such conditions -- that is, the claims recite a method of providing an indication (not a definitive diagnosis) of the relative likelihood that a human will develop such a condition. However, applicant's arguments are found not persuasive because "the assessment" of undesirable bone density condition by genetic testing is "the diagnostic" of an undesirable bone density using the same genetic test or methodology. Therefore the assessment and diagnostic via genetic testing are interchangeable terminologies, as both require identical materials and methods.

The applicant argues that they are the first to recognize that the susceptibility of an individual for undesirable bone density conditions can be assessed by looking at the cumulative effects of disorder-associated polymorphisms in genes whose products have important roles in bone density bone density (e.g., in two or more of the genes disclosed in the specification). The applicant argues that in order establish non-enablement on the grounds of inoperability, the office must provide a credible, art-supported reason why a skilled artisan in this field would not find the applicants' assertions of operability to be credible. The applicant argues that a skilled artisan in this field would understand, in view of the explanations provided in the specification, that the claimed methods can be used to assess relative susceptibility to such conditions.

However, applicant's arguments are found not persuasive because the earlier office action provides clear evidence that the osteoporosis (an undesirable bone density condition) is a common disorder with a complex patho-physiology involving both endogenous and environmental factors. The family and twin studies have shown that genetic factors play an essential role in bone mass regulation and that apart from rare instances the heritability of bone mineral density and osteoporosis is polygenic. An important problem with most candidate gene studies is small sample size, and this has led to conflicting results in different populations. Even though candidate gene association studies are relatively easy to perform, the disadvantages include the possibility of false positive (or false negative) results due to confounding factors and population stratification. The applicant failst o consider that the demonstration of an association between a candidate gene and BMD does not necessarily mean that the

gene is causally responsible for the effect observed. Associations can also occur as the result of linkage disequilibrium with a causal gene situated nearby on the same chromosome. (See Ralston J Clin Endocrinol Metab. 87(6):2460-6 2002, Zajikova et al Endocr Regul. 37(1):31-44, 2003). Thus the burdens shifts to applicant to establish that the one skilled in the art would able to practice the invention as claimed in view of limited amount of guidance provided in the specification without further undue amount of experimentation. For example the speciation as filed fails to disclose oligonucleotides that identifies SNPs of any and all DAPs encompasses by the scope of invention as claimed.

At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "**Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art.**" See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). Thus considering the state of the art which teaches that demonstration of an association between a candidate gene and BMD does not necessarily mean that the gene is causally responsible for the effect observed, the specification as filed fails to disclose that assessing the polymorphisms in any combinations of DAPs is predictive of diagnosing any undesirable bone density condition (i.e. osteophorosis or high bone mass). The specification even fails to establish any bone density condition (i.e. osteophorosis or high bone mass) associated with all polymorphic gene associated with Vitamin D receptor and Interleukin-6 genes. Similarly, the specification fails to provide any evidence that establishes the association of any undesirable bone density conditions associated with the occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor and a cytosine residue at position -174 of the interleukin-6 gene promoter. The disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Considering the instant specification it is even unclear how bone density is effected by the presence of these SNPs. In addition, the specification fails to provide any evidence, which establishes that

assessment of these SNPs in combination would be a better predictor of assessing an undesirable bone density as compared to identification of a single SNP.

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "**a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.**"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of skill. The specification fails to enable one skill in the art to practice the invention as claimed without further undue amount of experimentation.

In instant case assessing any undesirable bone density conditions by genetic analysis of any two known DAPs is not considered routine in the art and without sufficient evidence that combination of DAPs would be a better predictor of assessing an undesirable bone density as compared to identification of a single SNP the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Audi et al (Horm. Res. 51:105-123, 1999).

The scope of instant claims encompasses method of assessing relative susceptibility of a human to an undesirable bone density by assessing polymorphism in Vitamin D Receptor and Interleukin-6.

Audi teaches candidate genes for genetic determination of bone density (see abstract, page 106 table-1, page 107, col.1, page 115, col.1). Thus given the broadest reasonable interpretation to the invention as claimed the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**

SUMESH KAUSHAL
PRIMARY EXAMINER
ART UNIT 1633